REMARKS

Claims 1 and 5-13 currently appear in this application. The Office Action of august 9, 2007, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Amendments

The limitations of claim 3 have been incorporated into claim 1. Claims 2-4 have been cancelled.

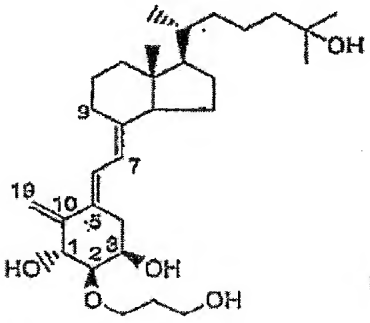
New claim 11 specifies that (5E,7E)-(1R, 2R, 3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol (trans form of ED-71) is an **isolated** compound. New claims 12 and 13, which are directed to a method for suppressing generation of degradation products, are supported by the entire specification, particularly paragraphs 0007-0011 and 0036.

Art Rejections

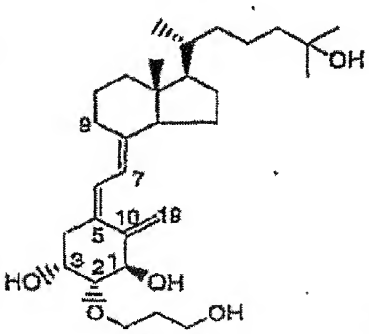
Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Katsushito et al. It is assumed that this is Miyamoto et al., *Chem. Pharm. Bull.* **41(6)**: 11121-1113, 1993.

This rejection is respectfully traversed. As recited in claim 1 of the present application, (5Z,7E)-(1R, 2R, 3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol, ED-71, can decompose to 6E-(1R, 2R, 3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5(10), 6, 8, (9)-triene-1,3,25-triol, **tachysterol of ED-71** and/or (5E,7E)-(1R, 2R, 3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol, the **trans form of ED-71**.

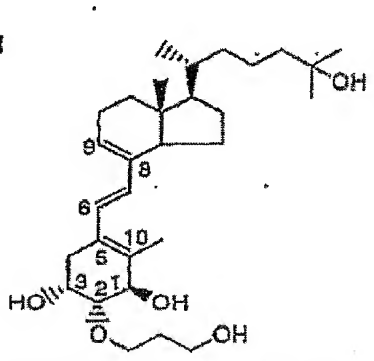
These compound names and their chemical structures are shown in the present specification, for example, in paragraphs 0007-0011 and 0028-0032. The chemical formulas are provided below:



1: Trans form of ED-71
(5E form)



2: ED-71
(5Z form)



3: Tachysterol form of ED-71

As is apparent for the chemical formulae, these three compounds differ in the configuration at the 5-position or in the locations of existing double bonds. Furthermore, they actually exist as **separate** compounds. For example each of the compounds can be separated from the other by, *e.g.*,

chromatography, as shown in Figures 1 and 2 of the present application.

Claim 10 is directed to the trans form of ED-71, that is, the 5E form. However, the compound 3 of Kaktsuhito is ED-71, which corresponds to formula 2, the 5Z-form, shown above. This is a different, geometric isomer of the trans form of ED-71, which is the 5E-form.

Claim 10 is rejected under 35 U.S.C. 102(e) as being anticipated by Yamuchi, U.S. patents 6,831,183 and 7,235,679.

This rejection is respectfully traversed. Yamauchi discloses the compound of the 5E-form, which is evident from formula I in the abstract of each patent and formula IX set forth in column 8 of each of these patents. As claim 10 is directed to the 5Z, the trans form of ED-71, which is a different compound, it is respectfully submitted that the presently claimed compound is novel over the cited references.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., WO 03 047595, Miyamoto et al., and Kaktsuhito, *Chem. Pharm. Bull.* These references are said to teach vitamin D preparations containing ED-71, fat and oil, and an antioxidant which embraces the presently claimed invention.

This rejection is respectfully traversed. Chen states at paragraph 0056, "The pharmaceutical compositions of

the present invention may further comprise one or more additives. Additives that are well known in the art include, e.g., …antioxidants (e.g., ascorbyl palmitate, butyl hydroxyl anisole (BHA). Butyl hydroxyl toluene (BHT) and tocopherols, e.g. α-tocopherol (vitamin E)…" However, it was general technical knowledge at the time of completion of the present invention that antioxidants are added to suppress generation of oxides, that is, to prevent oxidation of compounds in a system. Thus, one skilled in the art would have assumed that the antioxidants in Chen were provided to prevent generation of oxides.

On the other hand, the decomposition products to be suppressed in the presently claimed compositions are the trans form of ED-71 and the tachysterol form of ED-71. These decomposition products are not oxides of ED-71, but rather are isoforms of ED-71 (please refer to the structural formulae presented *supra*). These decomposition products have neither an increased number of oxygen atoms nor a reduced number of hydrogen atoms, which would be the result of oxidation of ED-71. However, the antioxidant in the ED-71 composition suppresses generation of the trans form and the tachysterol form of ED-71, as shown in Examples 2-6 of the present specification.

Compound 3 in Kaktsuhito is ED-71 corresponding to the 5Z-form shown in formula 2 above. This is a different, geometric isomer of the trans form of ED-71, which is the 5E-form.

Miyamoto only discloses vitamin D_3 compounds of the **5Z-form**. This is clear from the contents of the specification as a whole, for example, from the chemical formula set forth in claim 1 and the abstract, which show a compound of the 5Z-form. Further, Miyamoto failed to disclose any compounds of the 5E-form. Therefore, Example 13 should be construed to disclose only ED-71 in the 5Z-form. Further, at column 9, lines 31-32, Miyamoto describes that the compound of Example 13 is produced from Compound 1, in which R_2 is OH. According to the description in column 2 of Miyamoto, compound 1 is processed to vitamin D_3 derivatives represented by formula (I), having the **5Z-configuration**. This is also shown in formula (I) set forth in column 1. This further supports the assertion that the compound of Example 13 has a 5Z-configuration, and is a different compound from the compound claimed herein.

The Yamauchi patents disclose ED-71, a compound of the 5E-form, as can be seen from formula (I) in the abstract and formula (IX) set forth in column 8.

The Examiner alleges at page 10, lines 3-5 of the Official Action, that the degradation product would be present in a composition containing ED-71. The prior art does not teach the names of the degradation compounds, but the composition would inherently contain degradation products. However, claim 11 recites **isolated** trans form of ED-71. There is nothing that would motivate one skilled in the art to isolate the trans form of Ed-71.

Indeed, Kaktsuhito discloses in the experimental section (please refer to page 1113) that vitamin D_3 compounds, including ED-71, were dissolved in medium chain triglycerides (MCT) and orally administered to rats. Further, Miyamoto discloses that the vitamin D_3 compound of Example 4 was dissolved in ethanol and administered intravenously to animals (column 3, lines 20-24), and that the vitamin D_3 compounds of Examples 4 and 6 were dissolved in MCT and orally administered to rats (column 3, lines 49-54). There is nothing in this disclosure that describes or suggests the possibility of the existence of specific decomposition products, let alone isolation of such substances.

Contrary to the Examiner's remarks, it is respectfully submitted that ED-71 preparations do not necessarily inherently contain the decomposition product, the trans form of ED-71. In support of this, attached hereto is a

copy of *J. Am. Chem. Soc.*, 1981, **103**:6781-6783. This article shows in Figure 1 of page 6782 that conversion of vitamin D_3 to its trans form (indicated as 5-6 trans D_3) can be driven by light ($h\gamma$). Thus, it was general technical knowledge at the time of completion of the present invention that generation of a trans form of vitamin D_3, including ED-71, requires light. However, generally vitamin D_3 preparations are stored in a light-shielding container. Thus, those skilled in the art would have assumed that, under conventional storage conditions, the trans form of ED-71 cannot be generated. In fact, in Example 1 of the present specification, the trans form of ED-71 was not generated unless an ED-71 preparation was subjected to a chemically special reaction condition. On the other hand, although it would not have been considered that the trans form can be generated under the storage conditions of Examples 2-6, the trans form was actually isolated and identified in the examples.

As noted above, the trans form of ED-71 is not necessarily generated and contained in an ED-71 preparation, and thus it would not have been obvious for those skilled in the art to detect and isolate the trans form from an ED-71 preparation.

The trans form of ED-71 has a differentiation-inducing activity that is almost 20 time higher than that of

the parent compound, ED-71. This is evidence of unexpected properties of the trans form over the cis form.

From the above, it is clear that none of the cited references discloses or suggests the trans form of ED-71. Therefore, one skilled in the art could not have obtained the trans form from reading the cited references. Accordingly, it is respectfully submitted that the trans form of ED-71 as claimed herein is novel over any of the cited references.

Double Patenting

Claim 10 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending application No. 11/751,179.

This rejection is respectfully traversed. Application 11/751,179 only claims the tachysterol form of ED-71 represented by formula III of the '179 application. As noted above, this compound is represented by formula 3 above. Claim 10 is directed to the 5E, or trans, form of ED-71, not to the tachysterol form of ED-71. Since these compounds are not the same, it is respectfully submitted that there can be no double patenting.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By: /Anne M. Kornbau/
Anne M. Kornbau
Registration No. 25,884

AMK:srd
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\Y\YUAS\Katsuki2\Pto\2008-01-07Amendment.doc